

WEST Search History

DATE: Tuesday, April 08, 2003

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
<i>DB=USPT,PGPB,JPAB,EPAB; PLUR=YES; OP=OR</i>			
L16	L15 and profilaggrin\$	2	L16
L15	L14 and antibod\$	967	L15
L14	L13 and (carrier or label\$)	979	L14
L13	L12 and "rheumatoid arthritis"	985	L13
L12	L10 and (arginine or citrulline)	4656	L12
L11	L10 and l1	6	L11
L10	L9 or l2 or l3 or l4 or l5 or l6 or l7 or l8	12614	L10
L9	((((424/185.1)!..CCLS.))	1156	L9
L8	((((424/184.1)!..CCLS.))	1665	L8
L7	((((424/184)!..CCLS.))	0	L7
L6	((((530/403)!..CCLS.))	699	L6
L5	((((530/350)!..CCLS.))	9941	L5
L4	((((436/516)!..CCLS.))	243	L4
L3	((((436/506)!..CCLS.))	269	L3
L2	((436/509)!..CCLS.)	138	L2
L1	filaggrin\$ or antifilaggrin\$	89	L1

END OF SEARCH HISTORY

Connecting via Winsock to Dialog

Logging in to Dialog

Trying 31060000009999...Open

DIALOG INFORMATION SERVICES

PLEASE LOGON:

ENTER PASSWORD:

Welcome to DIALOG

Dialog level 02.12.60D

Last logoff: 07apr03 12:14:03

Logon file405 08apr03 12:27:07

*** ANNOUNCEMENT ***

-File 515 D&B Dun's Electronic Business Directory is now online completely updated and redesigned. For details, see HELP NEWS 515.

-File 990 - NewsRoom now contains October 2002 to present records.
File 993 - NewsRoom archive contains 2002 records from January 2002-September 2002. To search all 2002 records, BEGIN 990,993 or B NEWS2002

-Alerts have been enhanced to allow a single Alert profile to be stored and run against multiple files. Duplicate removal is available across files and for up to 12 months. The Alert may be run according to the file's update frequency or according to a custom calendar-based schedule. There are no additional prices for these enhanced features. See HELP ALERT for more information.

-U.S. Patents Fulltext (File 654) has been redesigned with new search and display features. See HELP NEWS 654 for information.

-Connect Time joins DialUnits as pricing options on Dialog. See HELP CONNECT for information.

-CLAIMS/US Patents (Files 340,341, 942) have been enhanced with both application and grant publication level in a single record. See HELP NEWS 340 for information.

-SourceOne patents are now delivered to your email inbox as PDF replacing TIFF delivery. See HELP SOURCE1 for more information.

-Important news for public and academic libraries. See HELP LIBRARY for more information.

-Important Notice to Freelance Authors—
See HELP FREELANCE for more information

For information about the access to file 43 please see Help News43.

NEW FILES RELEASED

***Dialog NewsRoom - Current 3-4 months (File 990)

***Dialog NewsRoom - 2002 Archive (File 993)

***Dialog NewsRoom - 2001 Archive (File 994)

***Dialog NewsRoom - 2000 Archive (File 995)
***TRADEMARKSCAN-Finland (File 679)
***TRADEMARKSCAN-Norway (File 678)
***TRADEMARKSCAN-Sweden (File 675)

UPDATING RESUMED

***Delphes European Business (File 481)

RELOADED

***D&B Dun's Electronic Business Directory (File 515)
***U.S. Patents Fulltext 1976-current (File 654)
***Population Demographics (File 581)
***Kompass Western Europe (File 590)
***D&B - Dun's Market Identifiers (File 516)

REMOVED

***Chicago Tribune (File 632)
***Fort Lauderdale Sun Sentinel (File 497)
***The Orlando Sentinel (File 705)
***Newport News Daily Press (File 747)
***U.S. Patents Fulltext 1980-1989 (File 653)
***TOXNET data is added to ToxFile (F156)

New document supplier

IMED has been changed to INFOTRIE (see HELP OINFOTRI)

>>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
>>> of new databases, price changes, etc. <<<

* * * *

SYSTEM:HOME

Cost is in DialUnits

Menu System II: D2 version 1.7.8 term=ASCII

*** DIALOG HOMEBASE(SM) Main Menu ***

Information:

1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:

6. DIALOG(R) Document Delivery
7. Data Star(R)

(c) 2000 The Dialog Corporation plc All rights reserved.

/H = Help /L = Logoff /NOMENU = Command Mode

Enter an option number to view information or to connect to an online
service. Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).

? b 410

08apr03 12:27:07 User268147 Session D61.1

\$0.00 0.160 DialUnits FileHomeBase

\$0.00 Estimated cost FileHomeBase

\$0.00 Estimated cost this search

\$0.00 Estimated total session cost 0.160 DialUnits

File 410:Chronolog(R) 1981-2003/Mar
(c) 2003 The Dialog Corporation

Set Items Description

? set hi %%%;set hi %%%

HIGHLIGHT set on as "

HIGHLIGHT set on as "

? b 5, 71, 155, 172

08apr03 12:27:20 User268147 Session D61.2

\$0.00 0.070 DialUnits File410

\$0.00 Estimated cost File410

\$0.04 TELNET

\$0.04 Estimated cost this search

\$0.04 Estimated total session cost 0.229 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 5:Biosis Previews(R) 1969-2003/Mar W5

(c) 2003 BIOSIS

*File 5: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.

File 71:ELSEVIER BIOBASE 1994-2003/Apr W1

Set Items Description

S1 72 "PEPTIDYLARGININE DEIMINASE"

S2 863 DEIMINASE?

S3 169 AU='SERRE G' OR AU='SERRE G V' OR AU='SERRE G.' OR AU='SER-
RE GUY'

S4 30 AU='SIMON MICHEL' OR AU='SIMON MICHELE'

S5 0 E 12-36

S6 10 S3 AND S2

6/9/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

(c) 2003 BIOSIS. All rts. reserv.

14147807 BIOSIS NO.: 200300141836

cDNA cloning, gene organization and expression analysis of human
peptidylarginine deiminase type I.

AUTHOR: Guerrin Marina; Ishigami Akihito; Mechin Marie-Claire; Nachat
Rachida; Valmary Severine; Sebbag Mireille; Simon Michel(a); Senshu
Tatsuo; Serre Guy

AUTHOR ADDRESS: (a)Department of Epidermal Differentiation and Rheumatoid
Autoimmunity, Toulouse-Purpan Pathophysiology Center, INSERM U563 - P.
Sabatier University (IFR30, INSERM-CNRS-P. Sabatier Universite-Centre
Hospitalier Universitaire), 37 Allee J. Guesde, 31073, Toulouse, France

**France E-Mail: msimon@cict.fr

JOURNAL: Biochemical Journal 370 (1):p167-174 15 February 2003 2003

MEDIUM: print

ISSN: 0264-6021

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Peptidylarginine deiminases (PADs) catalyse a
post-translational modification of proteins through the conversion of
arginine residues into citrullines. The existence of four isoforms of PAD
(types I, II, III and IV) encoded by four different genes, which are
distinct in their substrate specificities and tissue-specific expression,
was reported in rodents. In the present study, starting from epidermis
polyadenylated RNA, we cloned by reverse transcriptase-PCR a full-length
cDNA encoding human PAD type I. The cDNA was 2711 bp in length and

encoded a 663-amino-acid sequence. The predicted protein shares 75% identity with the rat PAD type I sequence, but displays only 50-57% identity with the three other known human isoforms. We have described the organization of the human PAD type I gene on chromosome 1p36. A recombinant PAD type I was produced in *Escherichia coli* and shown to be enzymically active. Human PAD type I mRNAs were detected by reverse transcriptase-PCR not only in the epidermis, but also in various organs, including prostate, testis, placenta, spleen and thymus. In human epidermis extracts, analysed by Western blotting, PAD type I was detected as a 70 kDa polypeptide, in agreement with its predicted molecular mass. As shown by immunohistochemistry, the enzyme was expressed in all the living layers of human epidermis, with the labelling being increased in the granular layer. This is the first description of the human PAD type I gene and the first demonstration of its expression in epidermis.

REGISTRY NUMBERS: 372-75-8: CITRULLINE

DESCRIPTORS:

MAJOR CONCEPTS: Molecular Genetics (Biochemistry and Molecular Biophysics)

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: human (Hominidae)

ORGANISMS: PARTS ETC: chromosome 1--p36; epidermis--integumentary system ; placenta--reproductive system; prostate--reproductive system; spleen--blood and lymphatics, immune system; testis--reproductive system; thymus--blood and lymphatics, endocrine system, immune system

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CHEMICALS & BIOCHEMICALS: citrulline; peptidylarginine deiminase type I

GENE NAME: human PAD type I gene (human peptidylarginine deiminase type I gene) (Hominidae)--analysis, expression

METHODS & EQUIPMENT: complementary DNA cloning--genetic techniques, laboratory techniques; gene expression analysis--genetic techniques, laboratory techniques; gene organization analysis--genetic techniques, laboratory techniques

MISCELLANEOUS TERMS: deimination; post-translational modification

CONCEPT CODES:

03502 Genetics and Cytogenetics-General

03508 Genetics and Cytogenetics-Human

10062 Biochemical Studies-Nucleic Acids, Purines and Pyrimidines

10064 Biochemical Studies-Proteins, Peptides and Amino Acids

15002 Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph Studies

15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies

16504 Reproductive System-Physiology and Biochemistry

17002 Endocrine System-General

17016 Endocrine System-Thymus

18504 Integumentary System-Physiology and Biochemistry

34502 Immunology and Immunochemistry-General; Methods

BIOSYSTEMATIC CODES:

86215 Hominidae

6/9/2 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

(c) 2003 BIOSIS. All rts. reserv.

12781188 BIOSIS NO.: 200000534811

Human peptidylarginine deiminase type I: Full-length cDNA cloning and expression analysis.

AUTHOR: Guerrin M(a); Ishigami A; Sebbag M(a); Senshu T; Serre G(a)

AUTHOR ADDRESS: (a)Department of Biology and Pathology of the Cell, Purpan
 School of Medicine, INSERM C/JF 9602-JFR 30, Toulouse**France
 JOURNAL: Journal of Investigative Dermatology 115 (3):p543 September, 2000
 MEDIUM: print
 CONFERENCE/MEETING: Abstracts for the 30th European Society for
 Dermatological Research Annual Meeting Berlin, Germany September 21-23,
 2000
 ISSN: 0022-202X
 RECORD TYPE: Citation
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 DESCRIPTORS:
 MAJOR CONCEPTS: Molecular Genetics (Biochemistry and Molecular
 Biophysics); Integumentary System (Chemical Coordination and
 Homeostasis)
 BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,
 Animalia
 ORGANISMS: human (Hominidae)--normal subjects
 BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans;
 Mammals; Primates; Vertebrates
 CHEMICALS & BIOCHEMICALS: peptidylarginine deiminase type I--
 epidermal expression analysis, full length complementary DNA cloning
 MISCELLANEOUS TERMS: Meeting Abstract
 CONCEPT CODES:
 03502 Genetics and Cytogenetics-General
 00520 General Biology-Symposia, Transactions and Proceedings of
 Conferences, Congresses, Review Annuals
 03508 Genetics and Cytogenetics-Human
 18504 Integumentary System-Physiology and Biochemistry
 BIOSYSTEMATIC CODES:
 86215 Hominidae

6/9/3 (Item 1 from file: 71)
 DIALOG(R)File 71:ELSEVIER BIOBASE
 (c) 2003 Elsevier Science B.V. All rts. reserv.

02275443 2003058819
 cDNA cloning, gene organization and expression analysis of human
 peptidylarginine deiminase type I
 Guerrin M.; Ishigami A.; Mechin M.-C.; Nachat R.; Valmary S.; Sebbag M.;
 Simon M.; Senshu T.; Serre G.
 ADDRESS: M. Simon, Dept. Epidermal Differentiation/R., INSERM U563 - P.
 Sabatier Univ., INSERM-CNRS-P. Sabatier Univ.-C., 37 allees J.
 Guesde, 31073 Toulouse, France
 EMAIL: msimon@cict.fr
 Journal: Biochemical Journal, 370/1 (167-174), 2003, United Kingdom
 PUBLICATION DATE: February 15, 2003
 CODEN: BJOA
 ISSN: 0264-6021
 DOCUMENT TYPE: Article
 LANGUAGES: English SUMMARY LANGUAGES: English
 NO. OF REFERENCES: 46

Peptidylarginine deiminases (PADs) catalyse a post-translational
 modification of proteins through the conversion of arginine residues into
 citrullines. The existence of four isoforms of PAD (types I, II, III and
 IV) encoded by four different genes, which are distinct in their substrate
 specificities and tissue-specific expression, was reported in rodents. In
 the present study, starting from epidermis polyadenylated RNA, we cloned by
 reverse transcriptase-PCR a full-length cDNA encoding human PAD type I. The
 cDNA was 2711 bp in length and encoded a 663-amino-acid sequence. The

predicted protein shares 75% identity with the rat PAD type I sequence, but displays only 50-57% identity with the three other known human isoforms. We have described the organization of the human PAD type I gene on chromosome 1p36. A recombinant PAD type I was produced in *Escherichia coli* and shown to be enzymically active. Human PAD type I mRNAs were detected by reverse transcriptase-PCR not only in the epidermis, but also in various organs, including prostate, testis, placenta, spleen and thymus. In human epidermis extracts analysed by Western blotting, PAD type I was detected as a 70 kDa polypeptide, in agreement with its predicted molecular mass. As shown by immunohistochemistry, the enzyme was expressed in all the living layers of human epidermis, with the labelling being increased in the granular layer. This is the first description of the human PAD type I gene and the first demonstration of its expression in epidermis.

DESCRIPTORS:

Citrulline; Deimination; Enzyme; Epidermis; Post-translational modification

CLASSIFICATION CODE AND DESCRIPTION:

84.1.3.1 - GENETICS AND MOLECULAR BIOLOGY / MOLECULAR GENETICS /
Modification and Restriction / DNA
84.1.13.2 - GENETICS AND MOLECULAR BIOLOGY / MOLECULAR GENETICS / Molecular
Biology Techniques / Cloning techniques and PCR
84.5.10.2 - GENETICS AND MOLECULAR BIOLOGY / EUKARYOTIC GENETICS / Human
Genetics / Enzymes and other proteins
89.8.7 - CELL AND DEVELOPMENTAL BIOLOGY / DEVELOPMENT (BY TISSUE AND ORGAN
SYSTEMS) / Skin and Appendages

MOLECULAR SEQUENCE DATABANK NUMBER:

GENBANK/AB010998/(REFERRED NUMBER)
GENBANK/AB030176/(REFERRED NUMBER)
GENBANK/AB033768/(SUBMITTED NUMBER)
GENBANK/AK026652/(REFERRED NUMBER)
GENBANK/NM013358/(SUBMITTED NUMBER)

6/9/4 (Item 2 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

01696791 2001069761

The major synovial targets of the rheumatoid arthritis-specific
antifilaggrin autoantibodies are deiminated forms of the alpha-and
beta-chains of fibrin

Masson-Bessiere C.; Sebbag M.; Girbal-Neuhausser E.; Nogueira L.; Vincent C.
; Senshu T.; Serre G.

ADDRESS: Prof. G. Serre, Lab. de Biol. Cellulaire/Cytologie, Ctr. Hosp.
Universitaire Purpan, Place du Dr Baylac, 31059 Toulouse, Cedex,
France

EMAIL: serre.g@chu-toulouse.fr

Journal: Journal of Immunology, 166/6 (4177-4184), 2001, United States

PUBLICATION DATE: March 15, 2001

CODEN: JOIMA

ISSN: 0022-1767

DOCUMENT TYPE: Article

LANGUAGES: English SUMMARY LANGUAGES: English

NO. OF REFERENCES: 49

IgG antifilaggrin autoantibodies (AFA) are the most specific serological
markers of rheumatoid arthritis. In epithelial tissues, they recognize
citrulline-bearing epitopes present on various molecular forms of
(pro)filaggrin. Histological analysis of rheumatoid synovial membranes with
an Ab to citrulline showed labeling of interstitial amorphous deposits and

mononuclear cells of various types. Immunochemical analysis of exhaustive sequential extracts of the same tissues showed that they contain several deiminated (citrulline containing) proteins. Among them, two proteins, p64-78 and p55-61, present in urea-DTT and guanidine extracts, were shown by immunoblotting to be specifically targeted by AFA. By amino-terminal sequencing the proteins were identified as deiminated forms of the alpha- and beta-chains of fibrin, respectively. Their identity was confirmed using several Abs specific for the Aalpha and/or to the Bbeta-chain of fibrin(ogen). Moreover, AFA-positive rheumatoid arthritis (RA) sera and purified AFA were highly reactive to the Aalpha- and Bbeta-chains of human fibrinogen only after deimination of the molecules by a peptidylarginine deiminase. Autoantibodies affinity purified from a pool of RA sera onto deiminated fibrinogen were reactive toward all of the epithelial and synovial targets of AFA. This confirmed that the autoantibodies to the deiminated Aalpha- and Bbeta-chains of fibrinogen, the autoantibodies to the synovial proteins p64-78 and p55-61, and, lastly, AFA, constitute largely overlapping autoantibody populations. These results show that deiminated forms of fibrin deposited in the rheumatoid synovial membranes are the major target of AFA. They suggest that autoimmunization against deiminated fibrin is a critical step in RA pathogenesis.

CLASSIFICATION CODE AND DESCRIPTION:

86.8.5.4 - IMMUNOLOGY AND INFECTIOUS DISEASES / IMMUNE RESPONSE DISORDERS /
Autoimmunity / Diagnosis and therapy

6/9/5 (Item 3 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE
(c) 2003 Elsevier Science B.V. All rights reserved.

01043412 1999010340

The epitopes targeted by the rheumatoid arthritis-associated antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues

Girbal-Neuhausser E.; Durieux J.-J.; Arnaud M.; Dalbon P.; Sebbag M.; Vincent C.; Simon M.; Senshu T.; Masson-Bessiere C.; Jolivet-Reynaud C.; Jolivet M.; Serre G.

ADDRESS: Prof. G. Serre, Lab. Biol. Cellulaire et Cytologie, Centre Hosp. Universitaire Purpan, Place du Dr Baylac, 31059 Toulouse Cedex, France

EMAIL: serre@cict.fr

Journal: Journal of Immunology, 162/1 (585-594), 1999, United States

PUBLICATION DATE: January 1, 1999

CODEN: JOIMA

ISSN: 0022-1767

DOCUMENT TYPE: Article

LANGUAGES: English SUMMARY LANGUAGES: English

NO. OF REFERENCES: 56

Antifilaggrin autoantibodies (AFA) are a population of IgG autoantibodies associated to rheumatoid arthritis (RA), which includes the so-called 'antikeratin' Abs and antiperinuclear factor. AFA are the most specific serological markers of RA. We previously showed that they recognize human epidermal filaggrin and other profilaggrin-related proteins of various epithelial tissues. Here, we report further characterization of the protein Ags and epitopes targeted by AFA. All the Ags that exhibit numerous neutral/acidic isoelectric variants were immunochemically demonstrated to be deiminated proteins. In vitro deimination of a recombinant human filaggrin by a peptidylarginine deiminase generated AFA epitopes on the protein. Moreover, two of three filaggrin-derived synthetic peptides with a citrulline in the central position were specifically and widely recognized by AFA affinity-purified from a series of RA sera. These

results indicate that citrulline residues are constitutive of the AFA epitopes, but only in the context of specific amino acid sequences of filaggrin. In competition experiments, the two peptides abolished the AFA reactivity of RA sera, showing that they present major AFA epitopes. These data should help in the identification of a putative deiminated AFA-inducing or cross-reactive articular autoantigen and provide new insights into the pathogenesis of RA. They could also open the way toward specific immunosuppressive and/or preventive therapy of RA.

CLASSIFICATION CODE AND DESCRIPTION:

86.8.5.2 - IMMUNOLOGY AND INFECTIOUS DISEASES / IMMUNE RESPONSE DISORDERS /

Autoimmunity / Human studies

6/9/6 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

14564273 22458323 PMID: 12416996

cDNA cloning, gene organization and expression analysis of human peptidylarginine deiminase type I.

Guerrin Marina; Ishigami Akihito; Mechin Marie-Claire; Nachat Rachida; Valmary Severine; Sebbag Mireille; Simon Michel; Senshu Tatsuo; Serre Guy

Department of Epidermal Differentiation and Rheumatoid Autoimmunity, Toulouse-Purpan Pathophysiology Center, INSERM U563 - P. Sabatier University (IFR30, INSERM-CNRS-P. Sabatier Universite-Centre Hospitalier Universitaire), Toulouse, France.

Biochemical journal (England) Feb 15 2003, 370 (Pt 1) p167-74,

ISSN 0264-6021 Journal Code: 2984726R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Peptidylarginine deiminases (PADs) catalyse a post-translational modification of proteins through the conversion of arginine residues into citrullines. The existence of four isoforms of PAD (types I, II, III and IV) encoded by four different genes, which are distinct in their substrate specificities and tissue-specific expression, was reported in rodents. In the present study, starting from epidermis polyadenylated RNA, we cloned by reverse transcriptase-PCR a full-length cDNA encoding human PAD type I. The cDNA was 2711 bp in length and encoded a 663-amino-acid sequence. The predicted protein shares 75% identity with the rat PAD type I sequence, but displays only 50-57% identity with the three other known human isoforms. We have described the organization of the human PAD type I gene on chromosome 1p36. A recombinant PAD type I was produced in *Escherichia coli* and shown to be enzymically active. Human PAD type I mRNAs were detected by reverse transcriptase-PCR not only in the epidermis, but also in various organs, including prostate, testis, placenta, spleen and thymus. In human epidermis extracts analysed by Western blotting, PAD type I was detected as a 70 kDa polypeptide, in agreement with its predicted molecular mass. As shown by immunohistochemistry, the enzyme was expressed in all the living layers of human epidermis, with the labelling being increased in the granular layer. This is the first description of the human PAD type I gene and the first demonstration of its expression in epidermis.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: *Hydrolases--genetics--GE; Amino Acid Sequence; Cloning, Molecular, DNA, Complementary; Epidermis--enzymology--EN; Hydrolases--chemistry--CH; Hydrolases--metabolism--ME; Molecular Sequence Data; RNA, Messenger--genetics--GE; Recombinant Proteins--chemistry--CH; Recombinant Proteins--genetics--GE; Recombinant Proteins--metabolism--ME; Sequence

Homology, Amino Acid; Substrate Specificity
Molecular Sequence Databank No.: GENBANK/AB033768; GENBANK/NM013358
CAS Registry No.: 0 (DNA, Complementary); 0 (RNA, Messenger); 0
(Recombinant Proteins)
Enzyme No.: EC 3. (Hydrolases); EC 3.5.3.- (peptidylarginine
deiminase type I)
Record Date Created: 20030206
Record Date Completed: 20030314

6/9/7 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

14506460 22458323 PMID: 12416996
cDNA cloning, gene organization and expression analysis of human
peptidylarginine deiminase type I.
Guerrin Marina; Ishigami Akihito; Mechin Marie-Claire; Nachat Rachida;
Valmary Severine; Sebbag Mireille; Simon Michel; Senshu Tatsuo; Serre
Guy
Department of Epidermal Differentiation and Rheumatoid Autoimmunity,
Toulouse-Purpan Pathophysiology Center, INSERM U563 - P. Sabatier
University (IFR30, INSERM-CNRS-P. Sabatier Universite-Centre Hospitalier
Universitaire), Toulouse, France.
Biochemical journal (England) Feb 15 2003, 370 (Pt 1) p167-74,
ISSN 0264-6021 Journal Code: 2984726R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
Subfile: INDEX MEDICUS

Peptidylarginine deiminases (PADs) catalyse a post-translational
modification of proteins through the conversion of arginine residues into
citrullines. The existence of four isoforms of PAD (types I, II, III and
IV) encoded by four different genes, which are distinct in their substrate
specificities and tissue-specific expression, was reported in rodents. In
the present study, starting from epidermis polyadenylated RNA, we cloned by
reverse transcriptase-PCR a full-length cDNA encoding human PAD type I. The
cDNA was 2711 bp in length and encoded a 663-amino-acid sequence. The
predicted protein shares 75% identity with the rat PAD type I sequence, but
displays only 50-57% identity with the three other known human isoforms. We
have described the organization of the human PAD type I gene on chromosome
1p36. A recombinant PAD type I was produced in Escherichia coli and shown
to be enzymically active. Human PAD type I mRNAs were detected by reverse
transcriptase-PCR not only in the epidermis, but also in various organs,
including prostate, testis, placenta, spleen and thymus. In human epidermis
extracts analysed by Western blotting, PAD type I was detected as a 70 kDa
polypeptide, in agreement with its predicted molecular mass. As shown by
immunohistochemistry, the enzyme was expressed in all the living layers of
human epidermis, with the labelling being increased in the granular layer.
This is the first description of the human PAD type I gene and the first
demonstration of its expression in epidermis.

Molecular Sequence Databank No.: GENBANK/AB033768; GENBANK/NM013358
Record Date Created: 20030206

6/9/8 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

11666499 99101527 PMID: 9886436
The epitopes targeted by the rheumatoid arthritis-associated

antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues.

Girbal-Neuhauser E; Durieux J J; Arnaud M; Dalbon P; Sebbag M; Vincent C; Simon M; Senshu T; Masson-Bessiere C; Jolivet-Reynaud C; Jolivet M; Serre G

Department of Biology and Pathology of the Cell, Institut National de la Sante et de la Recherche Medicale, Toulouse-Purpan School of Medicine, University Toulouse III, France.

Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Jan 1 1999, 162 (1) p585-94, ISSN 0022-1767 Journal Code: 2985117R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

Antifilaggrin autoantibodies (AFA) are a population of IgG autoantibodies associated to rheumatoid arthritis (RA), which includes the so-called "antikeratin" Abs and antiperinuclear factor. AFA are the most specific serological markers of RA. We previously showed that they recognize human epidermal filaggrin and other profilaggrin-related proteins of various epithelial tissues. Here, we report further characterization of the protein Ags and epitopes targeted by AFA. All the Ags that exhibit numerous neutral/ acidic isoelectric variants were immunochemically demonstrated to be deiminated proteins. In vitro deimination of a recombinant human filaggrin by a peptidylarginine deiminase generated AFA epitopes on the protein. Moreover, two of three filaggrin-derived synthetic peptides with a citrulline in the central position were specifically and widely recognized by AFA affinity-purified from a series of RA sera. These results indicate that citrulline residues are constitutive of the AFA epitopes, but only in the context of specific amino acid sequences of filaggrin. In competition experiments, the two peptides abolished the AFA reactivity of RA sera, showing that they present major AFA epitopes. These data should help in the identification of a putative deiminated AFA-inducing or cross-reactive articular autoantigen and provide new insights into the pathogenesis of RA. They could also open the way toward specific immunosuppressive and/or preventive therapy of RA.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: *Arginine--metabolism--ME; *Arthritis, Rheumatoid--immunology--IM; *Autoantibodies--biosynthesis--BI; *Epitopes--metabolism--ME; *Intermediate Filament Proteins--immunology--IM; *Protein Precursors--immunology--IM; *Protein Processing, Post-Translational--immunology--IM; Amino Acid Sequence; Amino Acid Substitution; Arthritis, Rheumatoid--blood--BL; Arthritis, Rheumatoid--metabolism--ME; Autoantibodies--blood--BL; Autoantibodies--metabolism--ME; Citrulline--metabolism--ME; Epidermis--immunology--IM; Epithelium--immunology--IM; Epithelium--metabolism--ME; Hydrolases--metabolism--ME; Intermediate Filament Proteins--genetics--GE; Intermediate Filament Proteins--metabolism--ME; Molecular Sequence Data; Peptide Fragments--chemical synthesis--CS; Peptide Fragments--immunology--IM; Peptide Fragments--metabolism--ME; Protein Precursors--genetics--GE; Protein Precursors--metabolism--ME; Recombinant Proteins--immunology--IM; Recombinant Proteins--metabolism--ME

Molecular Sequence Databank No.: GENBANK/AF043380

CAS Registry No.: 0 (Autoantibodies); 0 (Epitopes); 0 (Intermediate Filament Proteins); 0 (Peptide Fragments); 0 (Protein Precursors); 0 (Recombinant Proteins); 0 (filaggrin); 0 (profilaggrin); 372-75-8 (Citrulline); 74-79-3 (Arginine)

Enzyme No.: EC 3. (Hydrolases); EC 3.5.3.15 (protein-arginine deiminase)

Record Date Created: 19990121

Record Date Completed: 19990121

6/9/9 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

09373715 21136399 PMID: 11238669

The major synovial targets of the rheumatoid arthritis-specific antifilaggrin autoantibodies are deiminated forms of the alpha- and beta-chains of fibrin.

Masson-Bessiere C; Sebbag M; Girbal-Neuhausser E; Nogueira L; Vincent C; Senshu T; Serre G

Department of Biology and Pathology of the Cell, Institut National de la Sante et de la Recherche Medicale Contrat Jeune Formation 96-02, Toulouse-Purpan School of Medicine, University Toulouse III, Toulouse, France.

Journal of immunology (Baltimore, Md. - 1950)(United States) Mar 15 2001, 166 (6) p4177-84, ISSN 0022-1767 Journal Code: 2985117R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

IgG antifilaggrin autoantibodies (AFA) are the most specific serological markers of rheumatoid arthritis. In epithelial tissues, they recognize citrulline-bearing epitopes present on various molecular forms of (pro)filaggrin. Histological analysis of rheumatoid synovial membranes with an Ab to citrulline showed labeling of interstitial amorphous deposits and mononuclear cells of various types. Immunochemical analysis of exhaustive sequential extracts of the same tissues showed that they contain several deiminated (citrulline containing) proteins. Among them, two proteins, p64-78 and p55-61, present in urea-DTT and guanidine extracts, were shown by immunoblotting to be specifically targeted by AFA. By amino-terminal sequencing the proteins were identified as deiminated forms of the alpha- and beta-chains of fibrin, respectively. Their identity was confirmed using several Abs specific for the A alpha- and/or to the B beta-chain of fibrin(ogen). Moreover, AFA-positive rheumatoid arthritis (RA) sera and purified AFA were highly reactive to the A alpha- and B beta-chains of human fibrinogen only after deimination of the molecules by a peptidylarginine deiminase. Autoantibodies affinity purified from a pool of RA sera onto deiminated fibrinogen were reactive toward all of the epithelial and synovial targets of AFA. This confirmed that the autoantibodies to the deiminated A alpha- and B beta-chains of fibrinogen, the autoantibodies to the synovial proteins p64-78 and p55-61, and, lastly, AFA, constitute largely overlapping autoantibody populations. These results show that deiminated forms of fibrin deposited in the rheumatoid synovial membranes are the major target of AFA. They suggest that autoimmunization against deiminated fibrin is a critical step in RA pathogenesis.

Tags: Animal; Human; Support, Non-U.S. Gov't

Descriptors: *Arthritis, Rheumatoid--immunology--IM; *Autoantibodies--metabolism--ME; *Autoantigens--immunology--IM; *Fibrin--metabolism--ME; *Imines--metabolism--ME; *Intermediate Filament Proteins--immunology--IM; *Synovial Membrane--immunology--IM; Antigen-Antibody Reactions; Arthritis, Rheumatoid--pathology--PA; Autoantigens--chemistry--CH; Autoantigens--metabolism--ME; Epitopes--immunology--IM; Epitopes--metabolism--ME; Fibrin--chemistry--CH; Fibrin--immunology--IM; Fibrinogen--chemistry--CH; Fibrinogen--immunology--IM; Fibrinogen--metabolism--ME; Immunohistochemistry, Intermediate Filament Proteins--chemistry--CH; Intermediate Filament Proteins--metabolism--ME; Peptide Fragments--chemistry--CH; Peptide Fragments--immunology--IM; Peptide Fragments--metabolism--ME; Rats; Synovial Membrane--chemistry--CH; Synovial Membrane--metabolism--ME

CAS Registry No.: 0 (Autoantibodies); 0 (Autoantigens); 0 (Epitopes); 0 (Imines); 0 (Intermediate Filament Proteins); 0 (Peptide

Fragments); 0 (filaggrin); 9001-31-4 (Fibrin); 9001-32-5 (Fibrinogen)
Record Date Created: 20010312
Record Date Completed: 20010517

6/9/10 (Item 1 from file: 172)
DIALOG(R)File 172:EMBASE Alert
(c) 2003 Elsevier Science B.V. All rts. reserv.

02896157 EMBASE No: 2003094195
cDNA cloning, gene organization and expression analysis of human
peptidylarginine deiminase type I
Guerrin M.; Ishigami A.; Mechin M.-C.; Nachat R.; Valmary S.; Sebbag M.;
Simon M.; Senshu T.; Serre G.
AUTHOR E-MAIL: msimon@cict.fr
M. Simon, Dept. Epidermal Differentiation/R., INSERM U563 - P. Sabatier
Univ., INSERM-CNRS-P. Sabatier Univ.-C., 37 allees J. Guesde, 31073
Toulouse France
Biochemical Journal (United Kingdom) 2003 VOL/ISS/PG: 370/1 (167-174)
CODEN: BJOA ISSN: 0264-6021
PUBLICATION DATE: 20030215
DOCUMENT TYPE: Article
NUMBER OF REFERENCES: 46
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH

Peptidylarginine deiminases (PADs) catalyse a post-translational modification of proteins through the conversion of arginine residues into citrullines. The existence of four isoforms of PAD (types I, II, III and IV) encoded by four different genes, which are distinct in their substrate specificities and tissue-specific expression, was reported in rodents. In the present study, starting from epidermis polyadenylated RNA, we cloned by reverse transcriptase-PCR a full-length cDNA encoding human PAD type I. The cDNA was 2711 bp in length and encoded a 663-amino-acid sequence. The predicted protein shares 75% identity with the rat PAD type I sequence, but displays only 50-57% identity with the three other known human isoforms. We have described the organization of the human PAD type I gene on chromosome 1p36. A recombinant PAD type I was produced in *Escherichia coli* and shown to be enzymically active. Human PAD type I mRNAs were detected by reverse transcriptase-PCR not only in the epidermis, but also in various organs, including prostate, testis, placenta, spleen and thymus. In human epidermis extracts analysed by Western blotting, PAD type I was detected as a 70 kDa polypeptide, in agreement with its predicted molecular mass. As shown by immunohistochemistry, the enzyme was expressed in all the living layers of human epidermis, with the labelling being increased in the granular layer. This is the first description of the human PAD type I gene and the first demonstration of its expression in epidermis.

AUTHOR KEYWORDS: Citrulline; Deimination; Enzyme; Epidermis; Post-translational modification